

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant : Xiaomao Li  
Appl'n. No. : 09/914,621  
Filed : December 26, 2001  
Title : NUCLEIC ACID RESPIRATORY SYNCYTIAL  
VIRUS VACCINES  
Grp./A.U. : 1636  
Examiner : Quang Nguyen  
Docket No. : 1038-1191 MIS/jb  
Date : September 16, 2003

**DECLARATION UNDER 37 CFR 1.131**

We, Xiaomao Li, Mary E. Ewasyshyn, Suryaprakash Sambhara and Michel H. Klein, respectively of 77 Harbour Square, Apt. 3701, Toronto, Ontario, Canada, M5J 2S2; Apt. 1411, 120 Promenada Circle, Thornhill, Ontario, Canada, L4J 7W9; 50 Harness Circle, Markham, Ontario, Canada, L3S 1Y1; and 54 Strathgowan Avenue, Toronto, Ontario, Canada, M4N 1B9, declare as follows:

1. We are the inventors named in this application.
2. We are also co-authors, along with others, of a scientific paper entitled "Protection against Respiratory Syncytial Virus Infection by DNA Immunization" (Li et al) published in J. Exp. Med., Vol. 188, Number 4, August 17, 1998, a date which predates the first filing of the subject matter claimed in this application (i.e. March 5, 1999) by less than one year.
3. The Li et al paper describes work performed in developing a plasmid vector expressing RSV F protein and results showing that such plasmid vector was as effective as live RSV in mice at inducing neutralizing antibody and cytotoxic T lymphocyte responses, protection against infection and high mRNA expression of lung interferon  $\gamma$  after viral challenge.

Application No. 09/914,621

2

4. The present invention is directed towards improved constructs in which nucleotides encoding the endogenous signal peptide are replaced by nucleotides encoding a heterologous signal peptide which enhances the level of expression of RSV F protein in the host. The enhanced expression levels lead to improved immunogenicity of the vector at the same dosage levels as described in Li et al for vectors having the autologous signal peptide sequence. Complete protection was obtained in the absence of cardiotoxin pretreatment under conditions where pretreatment with cardiotoxin was required for the pXL2 construct described in Li et al to confer complete protection.

5. The Li et al reference contains the statement:

"Treatment of muscle tissue with cardiotoxin before immunization with DNA F vectors was found to improve homogeneity of the anti-F antibody responses among different mice of the same group. However, our more recent results indicate that the pretreatment step can be eliminated after further modification of the vector using a more effective signal peptide for enhanced F protein expression/secretion (data not shown)". (page 684, right hand column)

The last sentence of the quotation refers to the subject matter of this application. The data referred to in the last sentence and the modified vector referred to must have existed prior to the date of the article for the statement to be made. Accordingly, to the extent that the statement refers to the present invention, the present invention was made by us prior to the date of the article.

6. In addition to ourselves, the paper names Cindy Xin Li, Mark Parrington, Judy Caterini, Olive James, George Cates and Run-Pan Du as co-authors. None of these persons made any inventive contribution to the present invention.

7. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge

Application No. 09/914,621

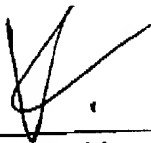
3

that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Declared at

TORONTO

on 6 day of Feb, 2002.4



Xiaomao Li

Declared at

on day of , 2003.

Mary E. Ewasyshyn

Declared at

on day of , 2003.

Suryaprakash Sambhara

Declared at

on day of , 2003.

Michel H. Klein

Feb-03-04 11:16am From-SIMBAS

T-876 P.018/024 F-663

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Application No. 09/814,821

2

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T-876 P.020/024 F-663

Application No. 09/914,621

3

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Declared at \_\_\_\_\_ on \_\_\_\_\_ day of \_\_\_\_\_, 2003.

\_\_\_\_\_  
Xiaomao LI

Declared at \_\_\_\_\_ on \_\_\_\_\_ day of \_\_\_\_\_, 2003.

\_\_\_\_\_  
Mary E. Ewasyszyn

Declared at Atlanta, Ga on 4<sup>th</sup> day of February, 2004

\_\_\_\_\_  
Suryaprakash Sambhara

Declared at \_\_\_\_\_ on \_\_\_\_\_ day of \_\_\_\_\_, 2003.

\_\_\_\_\_  
Michel H. Klein

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T-878 P.018/024 F-653

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Feb-03-04 11:18am From-SIMBAS

T-878 P.019/024 F-663

Application No. 09/914,921

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T-876 P.020/024 F-883

Feb-03-04 11:16am From-SIMBAS

Application No. 09/914,521

3

that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Declared at

on day of , 2003.

Xiaomao Li

Declared at

on 29<sup>th</sup> day of July, 2003.

M. Ewasyshyn  
Mary E. Ewasyshyn

Declared at

on day of , 2003.

Suryaprakash Sambhara

Declared at

on 21<sup>st</sup> day of July, 2003.

Michel H. Klein